Clinical Evaluation of Trikatu and Kumari as Hypolipidemic Drug

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ABSTRACT

Urbanization is characterized by a marked increase in the intake of energy-dense foods, a decrease in physical activity, and a heightened level of psychosocial stress, all of which promote the development of dysglycemia, hypertension, and dyslipidemia. Nowadays, dyslipidemia is a very much common disorder and it is the main disposing factor for the atherosclerosis, and the atherosclerosis is the main pathogenesis factor for Coronary heart disease (CHD) and Cardiovascular disease (CVD). CHD is the most prevalent cause of death and disability in both developed as well as developing countries. Ayurvedic classics have mentioned many efficacious herbs which work on digestion and metabolism. This clinical trial was done to evaluate the effect of Trikatu (Piper longum, Piper nigrum and Zingiber officinale) powder and Kumari (Aloe vera) pulp in the patients of dyslipidemia. 102 patients of dyslipidemia were selected and randomly divided into three groups - A, B and C of 34 patients each. The patients of group A, i.e. placebo group were administered two capsules of 500mg filled with wheat flour orally twice a day with Luke warm water. The patients of group B were treated with Trikatu powder 2 gm. BD with Luke warm water and the patients of group C treated with Trikatu powder 2 gm with 20 gm Aloe vera pulp. The duration of the trial was 3 months, with monthly follow up. Analysis of overall effect of trial drugs on subjective & objective parameters of all the three groups revealed that the results of Group C were highly significant (p<.001).

Key words: Aloe vera, Dyslipidemia, Lipid profile, Medoroga, Obesity, Trikatu

INTRODUCTION

Ayurveda, the Indian system of medicine can be aptly defined as the science of life or science of healthy living. The origin of Ayurveda can be traced beyond the Vedic period, i.e. about 5000 BC. [1] The whole philosophy of Ayurveda is based on achieving, maintaining and promoting positive health. The equilibrium of various structural and functional units of the body named as dosha (the medical humors as per Ayurveda), dhatu (tissues), mala (metabolic wastes), and more importantly the mind results in the state of health, whereas their disequilibrium causes disease. Correction of disturbance of milieu interior is the aim of the Ayurvedic management. [2]

Dyslipidemia is a very common metabolic disorder in these days due to the irregular diet habits, quality of food, lack of physical exercise added with stressful life style and other factors that lead to higher or fluctuating levels of the free fatty acids. All these are collectively responsible for altering the metabolic activities of the body, and these factors lead to change in lipid profiles particularly and more importantly, change in ratio of HDL (High Density Lipoprotein) and LDL (Low Density Lipoprotein). Lipid disorders may be associated with various disorders of different etiology like obesity, diabetes mellitus, myxoedema, hypopituatrism, nephrosis, etc. and this augments the major complications of lipid disorders as atherosclerosis, cardiovascular diseases (CVD) and coronary heart disease, which are in fact the major causes for mortality and morbidity not only in western countries but in India too. According to WHO (2002), in 2001 there were 7.3 million deaths and 58 million disability adjusted life years (DALYs) lost due to CHD worldwide. As it has long been known that lipid abnormalities are the major risk factors for premature coronary artery disease (CAD), South Asians around the globe have the highest rates of CAD. According to National Commission on Macroeconomics and Health (NCMH), a Government of India undertaking, there would be around 62 million patients with CAD by 2015 in India and of these, 23 million would be younger than 40 years of age. [3]

Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs), or both, or a low HDL level that contributes to the development of atherosclerosis. Because fats are practically

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insoluble in plasma water, they must circulate in the blood stream bound to soluble proteins known as lipoproteins. Plasma lipoproteins occur in four major forms which are:-
1. HDL that are also called alpha lipoproteins.
2. LDL that are also called beta lipoproteins.
3. VLDL that are also called alpha 2 or pre- beta lipoproteins.
4. Chylomicrons.

Usually we observe that obesity is the most common cause of dyslipidemia. A linear relationship has been established between obesity and dyslipidemia. The Ayurvedic texts have mentioned dyslipidemia as Medoroga or disorder arising due to vitiation of meda dhatu (lipsids and fat) and the related complications. [4] Ayurveda, expounds its concept to the disproportionate increase of one particular Dhatu i.e. Medas which creates obstruction in the Srotas (body pathways) and results in an impairment of Agni (metabolism) which is concerned with intermediary metabolism. Moreover, Sushruta has emphasized on metabolic disturbances in the etiopathogenesis of Sihaudya (obesity). He has clearly indicated that under certain conditions, the predominantly madhura (sweet) substances absorbed from the intestine circulate in un-metabolised form known as Ama rasa which is converted into Meda. The latter therefore, accumulates in the body and contributes to Medoroga, [5] i.e. dyslipidemia.

Of the various complications and sequelae of MedoRoga, dyslipidemia has been gaining much medical attention, and emphasis is being laid on procurement of a safe and effective drug. Modern medicine has come up with several drugs like Lovastin, Colestipol, Neomycin, Clofibrate, Cholestyramine etc. which act either by blocking the formation of different lipids or cholesterol at various stages in the biosynthetic pathway, or by increasing the fecal excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids. But it is unfortunate that none of them are free from toxicity and may cause only a stationary excretion of cholesterol or bile acids.

Sushruta states that Virakshana (dry), Medoghana (reduces lipids and fat) and Chedaniya or Srot-visisdhanjaya (drugs which forcefully detach unwanted metabolic waste and thus helps open the channels) substances can be used in the treatment of Medoroga, [7] as they act against deposition of lipids in body and help to clean off the blocked Srotasas.

Medoroga is one of the major diseases caused by excessive fatty diet and its metabolization which leads to production of cholesterol and triglycerides as an intermediary product. Thus these all are related to lipid metabolism. Yakrita (liver) is the major organ and acts as a chemical factory of the body. Liver synthesizes cholesterol and esters from lipids. Fatty acids are re-synthesized in the liver and released to circulation for being deposited in the adipose tissues. Thus, liver plays an important role in the metabolism of fat and lipids.

Drug review

Ayurvedic classics have mentioned many efficacious herbs which act on liver, digestive system and metabolism. Two such drugs, Trikatu (mixture of equal amount each of Piper nigrum, Piper longum and Zingiber officinale) and Ghritakumari (Aloe vera) have been taken for the present study on the grounds explained below.

The first drug in this study, Trikatu literally means three specific Katu dravyas (pungent substances), i.e. ginger, black pepper and long pepper, and coincidentally, these are used frequently as spices in Indian foods. Trikatu, has been described by Sushruta as Kaphamedoghana (alleviate Kapha dosha, viz. lipids & fats) and Deepana (appetizer), [8] which means that it removes the Kapha dosha and Meda and improves the Agni (metabolism). Vaghbhatta has also recommends Trikatu in the treatment of conditions involving both Meda and Kapha. [9] Sharangadhara has also described the pharmacological actions of Trikatu churna (powdered form) and labelled it as Sleshma-Medoghna, i.e. it alleviates Kapha dosha and Meda dosha (lipids disorders). [10]

The second drug, Ghritakumari (Aloe vera), is a Yakritottajaka drug i.e. it stimulates liver functions. Ayurvedic physicians usually use it in the treatment of liver disorders, digestive system and skin diseases. Bhavaprakasha has given the detailed descriptions of pharmacological actions and therapeutic indications of Trikatu and Ghritakumari, both. He recommends the drug Trikatu in treatment of Medoroga, Prameha (diabetes), Galma (abdominal tumor), Twaka roga (skin disease), etc. [11] According to him, Ghritakumari is Bhedana (helps breakdown the fecal matter) and Rasayana (rejuvenator), and indicated it for treatment of Yakrita-Pilha roga (liver & spleen disorders). [12]

Aims and Objectives of this study
1. To compare the clinical efficacy of Trikatu in the management of Hyperlipidemia, i.e. Medoroga.
2. To observe the synergic effect of Trikatu with Kumari pulp in the management of Hyperlipidemia, i.e. Medoroga.

MATERIALS AND METHODS

Study participants
A total of 102 patients of hyperlipidemia were registered from the OPD and IPD and randomly allocated into three groups. In the present work, 102 patients who fulfilled the diagnostic criteria of Medoroga (dyslipidemia) were selected. Out of which 20 patients had left the treatment at different stages. The remaining 82 patients, 25 patients in group A (Control), 27 patients in group B (Trikatu powder treated), 30 patients in group C (Trikatu powder with Aloe pulp treated group) completed the trial, whose data is being presented in this study. Informed consent of the participants was obtained and the study was approved by the local Institutional Ethics Committee.
Inclusion criteria
1. Patients aged >16 and <65 years.
2. Patient with clinical signs & symptoms of Medoroga as mentioned in the Ayurvedic and modern literatures.

Exclusion criteria
1. Patients aged < 16 years and > 65 years.
2. Dyslipidemia along with hypothyroidism, hormonal imbalance, cardiovascular diseases, hemiplegia, diabetes and severe hypertension.
3. Females with history of pregnancy and lactation.

Grouping and design
All the registered cases were divided randomly into four groups as follows-
Group A (n=34): is the control group. The patients of this group were given two placebo capsules BD with lukewarm water. Each capsule was filled with 500 mg wheat flour.
Group B (n=34): Patients of this group were administered Trikata churna 2 gm BD with lukewarm water.
Group C (n=34): Patients of this group were administered Trikata churna 2 gm and 20 gm Kumari pulp, BD with lukewarm water.

Diagnostic criteria for obesity
The diagnosis was based mainly upon the signs and symptoms mentioned in textbooks of Ayurvedic as well as modern medicine, such as –
- Ayurvedic parameters: Kshudra swasa (Dyspnoea), Daurgandhya (foul smell), Anga gaurava (heaviness in body), Ati kshudha (excessive hunger), Gatra sada (weakness), Sandhi shoola (pain in joints), Ati pipasa (excessive thrust), Snigdhaangata (unctuousness in body), Swedadhikya (excessive sweating).
- Modern parameters: Lipid profile, weight, BMI (Body mass index), and circumference of waist and hip.

Preparation of trial drugs
Trikatu powder and Kumari (Aloe vera) pulp both trial drugs were prepared in the Hans Pharmacy of Premnagar Ashram, Haridwar, Uttarakhand, as per the standard method of preparation described in “Sharangadhara Sambhita”.

Duration of the trial
3 months, with monthly follow-ups

Assessment criteria
The effect of therapy was assessed on the basis of improvement in following subjective and objective criteria.

Subjective criteria
A multi-dimensional scoring pattern was adopted for the signs and symptoms of Medoroga mentioned in Ayurvedic texts. The score for symptoms were assessed before and after the treatment and statistical analysis was undertaken. This assessment was done before starting the treatment and thereafter every month, till completion of the three months duration of therapy.

Objective criteria
1. Lipid profile was recorded before and after treatment.
2. Weight and BMI was recorded before and after treatment.
3. Circumference of hip and waist (in centimeters) were recorded before and after the treatment.

Assessment of overall effect of therapy
For an overall assessment of the therapy, following categories were taken into consideration:
1. Marked improvement: More than 60% improvement noted in signs and symptoms.
2. Moderate improvement: 40-60% improvement was noted in the signs and symptoms.
3. Mild Improvement: 20-40% improvement was noted in the signs and symptoms.
4. Unchanged: No effect in signs, symptoms and weight.

Data analysis
For statistical analysis of observations and results, paired ‘T’-test and independent ‘T’-test were used.

OBSERVATIONS AND RESULTS
- In the present series of 102 patients of dyslipidemia, maximum number of patients (64%) were in the age group of 30-50 years, males i.e. 67% & females i.e. 33%. 67% were belonged to service class. The most of the patient 44% were of the upper middle socioeconomic status.
- 75.53% patients of this series had mixed dietary habits, 75% were taking excess intake of Madhura, Guru (heavy), Snigdha (unctuous), Sheet (cold) and Shleshmala aahara (diet which increase Kapha dosha); 66% patients were living sedentary life style; and only 28% patients were having sound sleep.
- In present study, maximum patients (78.43%) were taking Guru dravas (heavy substances), followed by Snigdha (unctuous) [76.47%] and Sheeta dravas (substances of inherently of cold nature) [72.55%] in their diet.
- 85% of the patients reported different type of addictions like tobacco chewing, smoking & alcohol, and only 15% had no addictions.
- Maximum number of the patients (64.8%) had no family history.
- Prakriti (psychosomatic constitutions): In this series, maximum numbers of patients were of Kapha-Vata prakriti (50%) followed by Kapha-Pitta prakriti (35%) and Vata-Pitta prakriti (15%) and maximum number were of Tamasika Prakriti (50%), Rajasa (36%) and Satva Prakriti (14%) respectively.
- Maximum number of the patients 39% of Vishama Agni (irregular appetite) and 33% patients were of Tikshana Agni (excessive appetite), 44% patients were Krua-koshthi (constipation) and 40% patients were Madhyama-kosthi (regular bowel).
- Maximum numbers of patients (51%) were in the habit of Vishamasana (taking food at irregular time); Adhyasana (taking food at irregular time) 34 % and Samasana (taking food at irregular time) 15% were also reported.
In this study, all the patients showed the signs and symptoms of Medoroga, 68.65% patients were observed with Daurabalya (weakness) followed by 73.6% Angusaurva (heaviness in body) and 70.59% Kshudra sbwasa (dyspnoea). Among the other symptoms maximum Alaya (lascitude) was observed in 88.23% of patients, movement of Udara-Stana-Sfika Chalatva (movement of abdomen and buttocks on motion) in 71.56%, Snigdhagata (unctuousness in body) in 75.50% and Atikshudha (excessive appetite) in 65.69%.

The weight of 36.27% patients was noted in the range of 75-84 kg. and 35.29% were belonging in the range of 65-74 kg. As regards BMI, 48.04% patients were in the range of 25 to 29 kg/m², followed by 40.20% patients in the range of 30 to 34 kg/m².

Coming to abdominal and hip circumference, maximum range of abdominal girth was found in the range of 115-124 cm. in 33.34% patients and maximum hip circumference was in the range of 125-134cm. in 32.35% patients. 38.24% patients were having abdominal circumference in the range of 105-114cm and hip circumference in the range of 115-124 cm.

Family history of obesity was recorded in 50% patients.

Table 1: Comparative effect of Trial Drug and Placebo on Serum Lipids

<table>
<thead>
<tr>
<th>S t r o n g &amp; Symptoms</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±S.D. BT - AT</td>
<td>P Value</td>
<td>Mean±S.D. BT - AT</td>
<td>P Value</td>
</tr>
<tr>
<td>Serum Lipids (n = 82)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TC</td>
<td>194.71±4.31</td>
<td>192.80±4.28</td>
<td>194.12±4.43</td>
</tr>
<tr>
<td>LDL Cholesterol (n = 82)</td>
<td>104.63±3.06</td>
<td>106.14±3.50</td>
<td>104.35±3.25</td>
</tr>
<tr>
<td>HDL Cholesterol (n = 82)</td>
<td>41.56±2.18</td>
<td>41.28±2.43</td>
<td>41.57±2.24</td>
</tr>
<tr>
<td>Triglycerides (n = 82)</td>
<td>202.38±3.45</td>
<td>203.54±3.65</td>
<td>202.12±3.34</td>
</tr>
<tr>
<td>VLDL (n = 82)</td>
<td>35.62±2.97</td>
<td>35.82±3.12</td>
<td>35.68±2.94</td>
</tr>
<tr>
<td>Urea (n = 82)</td>
<td>0.41±0.65</td>
<td>0.42±0.65</td>
<td>0.41±0.65</td>
</tr>
<tr>
<td>Creatinine (n = 82)</td>
<td>0.24±0.24</td>
<td>0.25±0.25</td>
<td>0.24±0.22</td>
</tr>
</tbody>
</table>

Following charts depict the effect on various parameters in the three groups

Fig. 1: Effect on Serum Triglyceride in Dyslipidemia

Fig. 2: Effect of on Total Serum Cholesterol

Fig. 3: Effect on HDL Cholesterol in Dyslipidemia
Effects of trial drugs [Table 1 and 2], [Figure 1-11]

**Group A:** Overall effect of the placebo shows that there is a significant increase in dyslipidemia regarding their subjective and objective parameters.

**Group B:** *Trikatu churna* showed statistically significant (<0.01) reduction in weight, BMI and hip circumference and (p<0.05) in the symptoms of dyslipidemia. Regarding the biochemical parameters, a highly significant decrease was found in lipid profile, including HDL (p<0.001).

**Group C:** In patients on *Trikatu* powder along with *Aloe vera* pulp, as compared to *Trikatu* alone, statistically, a highly significantly reduction (p<0.001) was seen in weight and BMI, whereas a significant (p<0.01) reduction was observed in abdominal & hip girth (p<0.01) and symptoms of dyslipidemia. Regarding the biochemical parameters, a highly significant decrease was found in lipid profile including HDL (p<0.001).

The assessment of overall effect showed that *Trikatu* powder along with *Aloe vera* pulp provided remarkable relief in 30%, moderate improvement in 50% and mild improvement in 20% patients. In this study, 0% patients remain unchanged and none of the patient could achieve the 100% cure status. Thus overall study shows that among three groups, the effect in group C was found best. This shows that *Trikatu* with *Kumari* pulp is more effective than *Trikatu* alone as a hypolipidemic drug.

**DISCUSSION**

Excessive indulgence in oily, fatty and junk foods, sedentary life, irregular eating, late sleep and late morning waking, i.e. in nutshell, irregular modern lifestyle, coupled with lack of physical exercise and hereditary predisposition are the important factors responsible for dyslipidemia. A critical review of the data available in the Ayurvedic literatures, on subject of dyslipidemia in form of *Medoroga* brings out an amazing wealth of knowledge about the existing concept with regard to etiopathogenesis and treatment of dyslipidemia and its complications. In pathogenesis of *Medoroga*, *Kapha*, *Vayu*, *Meda* (fat/lipids) and *Medodhatvagni* (factor for metabolism of lipids and fats at tissue level) are the main responsible factors. As per Ayurveda, it is mainly by taking sweet natured excessive diet that the *Meda dhatu* increases in body and this obstructs the channels, thereby causing on one hand excess deposition of fat in the body and on the other hand due to hinderance...
in Srotasas, subsequent dhatus go on diminishing (i.e., due to malnutrition). It may thus be seen that the ancient Ayurvedic physicians had clearly understood the scientific process of digestion and metabolism. Ayurveda lays a great emphasis on the functional maintenance of Jatharagni (digestive fire), upon which depends the functions of subsequent Dhatuagni (factor for metabolism at tissue level) which is responsible for the nourishment of subsequent Dhatus one after another in a sequential order. Medoroga (lipid disorders) result due to excess/increase of meda due to hypo functioning of Medodhitwagni. Meda results in the obstruction of its channels and also causes hinderance at the microlevel in proper metabolism of fat.

Trikatu and Ghritakumari being of Katu, Tikta rasa and Katavipaka in nature, i.e. just opposite of Medodhatus, reduce the quantity of Medodhatus and also make the channels patent for easy conduction of nutrients for nourishment to following Dhatus. A number of popular preparations of Trikatu are being plasticized by the Ayurvedic physicians for treatment of many Kaphavatasa diseases, including Agnimandya (poor digestion) and Ama (undigested food and its toxic bye-products). By virtue of the therapeutical actions like Deepana (appetizer), Pachana (digestive), Rukshana (producing dryness), Lekhana (producing sliminess), Karshana (extraction), and Shoshana (absorption) etc., also along with its Tikshna (sharp), Laghu (light) and Sukshma (micro in size) properties, as a whole Trikatu reduces the quantity of Meda (which has the nature of Ama) and also makes the channels patent to carry on the nutrients to subsequent Dhatus as per the chronological order mentioned in Ayurveda. These pharmacological actions may be due to its chemical substance pipeline which enhances the secretion of digestive juices and might catalyze the functions of enzymes in small intestine too, i.e. it helps improve function of Jatharagni (digestive fire). Improvement of Jatharagni function, in total, also helps in a finer disintegration of nutrients, in turn helping maximum absorption for nourishing rest of the Dhatus, and thus also facilitates the function of Bhatagnis (metabolism). In short, Trikatu acts against the deposition of lipids and thus helps clean the eventually blocked channels.

The second drug, Ghritakumari is a Yakritatvajaka drug i.e. a potent cholagogue. Ayurvedic physicians usually use it in the treatment of liver disorders and digestive system. By virtue of Tikta rasa, Katu vipaka (bitter in post digestive taste), Bhedana karma (breaking down of fecal matter) and other obscure functional properties at macro to micro level, Ghritakumari facilitates the functions of Jatharagni (digestive fire), Dhatuagni and Bhatagni. As to how, it is much more effective for the treatment of Kapha predominant diseases like Medoroga i.e. dyslipidemia etc.; it plays the dual role of medicine as well as Rasayana (rejuvenator), as per the principles of Ayurveda. Moreover besides above properties, Ghritakumari is also a potent cholagogue i.e. enhances the secretion of bile from liver that plays its exclusive action in emulsification of fat. And due to its Sheeta virya (cold potency), Ghritakumari also suppresses the excessive secretion of Pitta and neutralizes excessive Pitta, which is acidic in nature in stomach, without hindering the very fundamental function of Agni.

So, Trikatu probably acts by blocking the formation of different lipids or cholesterol at various stages in the biosynthetic pathway, and Aloe vera acts by increasing the fecal excretion of cholesterol or bile acids. Because the main site of lipid metabolism is liver and the action of both these drugs is also seen on liver, so these trial drugs may be effective in controlling dyslipidemia; and because of being a Rasayana, they may also cause increase in the HDL cholesterol. Thus it is very obvious why Trikatu and Ghritakumari jointly summate the action of each other and hence have proved to be very effective drugs in the disease Medoroga vis a vis deranged fat metabolism, as seen in this study.

CONCLUSION

On the basis of this study we can conclude following points:

* Trikatu is very effective in reducing lipid profile, weight and BMI as well as in providing relief in all signs and symptoms; whereas Trikatu along with Kumari reduced lipid profile, weight and BMI in a more pronounced way, as well as provided better relief in all signs and symptoms compared to Trikatu alone.

It can be inferred from the present study that best effect of the trial drugs was seen with Trikatu and Ghritakumari together (Group C), which is most effective in reducing the overall lipid profile, with substantial gains related to subjective as well as objective parameters and that too, without any adverse effects.

REFERENCES


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